REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-4 were pending in this application when last examined and stand rejected.

The format of claim 1 has been changed to better conform with US practice. Support can be found in the claim as filed. For instance, claim 1 has been amended to recite "inoculating an animal with an expression vector expressing a fusion protein" instead of "inoculating an expression vector expressing a fusion protein to an animal." Step 1 of claim 1 was also amended to provide proper antecedent basis for the "antigenic protein" in step 2 by moving the "wherein the fusion protein" clause to step 1. Support can be found in the claim as filed.

Claim 1 has also been amended to clarify that "the antigenic protein is not naturally present on a cell surface." The antigenic protein is defined very broadly in the specification. The purpose of this amendment is limit the antigenic protein to those which are not naturally present on a cell surface as exemplified in the disclosure. For instance, Example 2 (on page 7) discloses the use of the nuclear protein HP10496 as the antigenic protein. This nuclear protein is not naturally present on a cell surface as it is localized in the nuclear spliceosome. In other words, it is antigenic protein that is not naturally present on a cell surface.

Therefore, no new matter has been added by this amendment.

Claims 3 and 4 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any canceled subject matter.

Claims 1-2 are pending upon entry of this amendment.

II. FOREIGN PRIORITY

In item 12(c)(1) on page 1 and item 1 on page 2, it was indicated that foreign priority has not been granted, because a certified copy of the priority document (JP 11/373389) has not been received.

It is respectfully submitted that a certified copy of the foreign priority document should have been provided by the International Bureau. Thus, kindly review the PTO file record for such and acknowledge the foreign priority claim. If necessary, Applicants will obtain and submit a certified copy of the priority document.

II. ANTICIPATION REJECTION

In item 3 on page 2 of the Office Action, claims 3 and 4 were rejected under 35 U.S.C. § 102(b) as anticipated by Yokoyama-Kobayashi (Gene, Vol. 228, No. 1-2, pp. 161-167, 1999).

The present amendment cancels the rejected claims, thereby obviating this rejection.

III. OBVIOUSNESS REJECTION

In item 5 on pages 2-3 of the Action, claims 1-4 were rejected under 35 U.S.C. § 103(a) as obvious over Scholler (US 2003/0008342) in view of Yokoyama-Kobayashi.

This rejection is respectfully traversed as applied to the amended claims.

To establish obviousness, three criteria must be met. First, the prior art references must teach or suggest each and every element of the claimed invention. M.P.E.P. § 2143.03. Second, there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claimed invention. M.P.E.P. § 2143.01. Third, the prior art must provide a reasonable expectation of success. M.P.E.P. § 2143.02.

Amended claim 1 calls for a method for producing an antibody, which method comprises inoculating an animal with an expression vector expressing a fusion protein comprising an antigenic protein fused with the C-terminal of a transmembrane domain, wherein when the fusion

protein is expressed, the N-terminal side of the transmembrane domain is located in the cell and the C-terminal side of the transmembrane domain is outside of the cell and the antigenic protein is outside of the cell, and further wherein the antigenic protein is not naturally present on the surface of a cell; and isolating an antibody against the antigenic protein from the animal and purifying the antibody.

As noted above, the antigenic protein of the claimed invention is defined very broadly in the specification. The purpose of the amendment to claim 1 is to limit the antigenic protein to those which are not naturally present on a cell surface as exemplified in the disclosure, and to thereby exclude the antigenic protein in the prior art.

Scholler and Yokoyama-Kobayashi fail to disclose or suggest using a fusion of a transmembrane domain and an antigenic protein that is not naturally present on a cell surface. Moreover, the cited references fail to provide a reasonable expectation of success for producing antibodies using a fusion between a transmembrane domain and an antigenic protein that is not naturally present on the surface of a cell.

Scholler relates to a technology aiming to elicit or enhance the titer of antibodies specific for a cell surface receptor antigen (SRA). Scholler suggests the use of transmembrane domain for causing the SRA to localize to the cell surface. See page 4, paragraph [0022]. However, Scholler does not present concrete examples for the use of a transmembrane domain in the claimed method for producing antibodies. Scholler merely contains an uncertain suggestion. Consequently, the only achievement assured of in Scholler is the expression of a naturally present SRA together with a first and second immune response altering molecules.

On the other hand, it was known in the art at the time of filing of the application that antibody titer decreases when using an antigenic protein, which has been converted into a membrane type by fusion with transmembrane domain. See page 2, lines 13-20 of the specification and the Boyle reference (Int. Immunol., vol. 9, no. 12, pp. 1897-1906, 1997) discussed therein. The Boyle reference was cited in the IDS of March 22, 2002. Prior to the

instant invention, it was reported that as an example of gene immunization, ovalbumin was fused to the downstream portion of a transmembrane domain of transferrin receptor to form a membrane type. When this fusion protein was injected intramuscularly or subcutaneously into mice in order to investigate the effect of the expression site of the antigenic protein on the efficacy of gene immunization, it was found that the antibody titer decreased, because the protein was converted into a membrane type.

Accordingly, there was no reasonable expectation of success in the art for producing antibodies using a fusion between a transmembrane domain and an antigenic protein that is not naturally present on the surface of a cell, because based on the state of the art and the uncertain suggestion in Scholler, such a fusion would decrease antibody production.

In contrast, Applicants succeeded in doing so by fusing a non-membrane type antigenic protein with the C-terminal of the transmembrane domain, thereby localizing the protein to the cell surface. It is respectfully submitted that this feature of the claimed invention was neither disclosed nor suggested by the cited prior art references, and there was no reasonable expectation of success in the prior art for modifying the prior art teachings for doing so.

Furthermore, amended claim 1 excludes the use of the antigenic protein disclosed in Scholler. The SRA in Scholler is an antigenic protein which is naturally present on a cell surface. Again, the amended claims call for using an antigenic protein that is not naturally present on a cell surface. Thus, Scholler fails to disclose or suggest each and every element of the claimed invention.

Yokoyama-Kobayashi fails to remedy the deficiencies in Scholler.

On page 3 of the Action, it was indicated that Yokoyama-Kobayashi discloses a vector encoding a fusion protein containing an artificially added transmembrane domain, wherein a protein is fused C-terminal to the transmembrane domain. The Office also indicated that Yokoyama-Kobayashi discloses that said vector can be used to produce a fusion protein that can be used to anchor a secreted molecule to the cell surface. However, Yokoyama-Kobayashi never

suggests using a fusion of a transmembrane domain and an antigenic protein that is not naturally present on a cell surface in the claimed method to produce antibodies.

In view of the above, the rejection of claims 1-4 under 35 U.S.C. § 103(a) over Scholler (US 2003/0008342) in view of Yokoyama-Kobayashi is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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